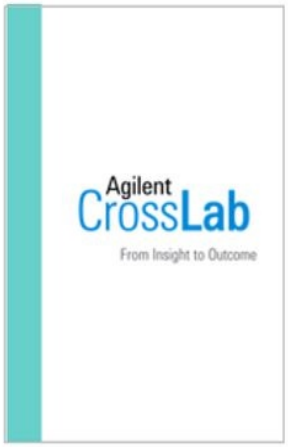
EQUIPMENT QUALIFICATION PLAN

Agilent CrossLab Compliance Services



EQP Name: DISS.02.54_PQ_R182R0_EQP

Service Type: PQ

Company Name: _____

Customer Name/Title: _____

EQP Filename: DISS.02.54_PQ_R182R0_eqp.eqp

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Test program as reflected in EQP agreement.

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Scope and Purpose

Overview

An Equipment Qualification Plan (EQP) documents the work performed during qualification services provided using the Agilent Automated Compliance Engine (ACE) software. The EQP must be approved before the work is performed (see customer responsibilities) and the results are reported in an Equipment Qualification Report (EQR), which documents the following.

-Tests performed during the qualification work
-Setpoints used (for example, wavelength, temperature, and flow settings, as applicable)
-Limits (acceptance criteria) applied to tests and setpoints
-Test descriptions and rationales for tests performed (these and test parameters are also reported EQR)
-Traceability of the Agilent qualification protocol

EQP PDF review documents support customer review and approval and are digitally produced directly from the electronic EQP contained within ACE. Two different EQP approval formats can be created.

-Concise: standard format, typically used for Agilent-recommended EQPs
-Tabular: expanded format, typically used for configured EQPs

Many customers approve the Agilent-recommended EQP in the concise format. The tests, setpoints, and limits applied are typically organized in a concise table format (see information below and the Operational Qualification (OQ) test suite). The table can also display which qualification tests can be configured, which Agilent designates as variance (see Glossary).

In a concise EQP approval document used for Agilent-recommended EQPs, the test, setpoints and parameters, and limits (as applicable) are displayed in a concise abbreviated format as shown below.

Key:	Fixed HPLC setpoints/limits	UHPLC setpoints	Variance allowed

Test	Setpoints and Parameters	Limits
CDS Logon Verification	N/A	Evidence of logon used to collect qualification data
Pump Flow Accuracy and Precision (> 400 bar)	Flow Rate 1: 0.500 ml/minute Flow Rate 2: 5.000 ml/minute Flow Rate 2: 2.000 ml/minute (G4220B) Flow Rate 2: 1.500 ml/minute (with ULD kit)	Accuracy Ò3.00% Precision RSD Ò0.50%

By design, ACE EQPs can be configured to align the qualification work to laboratory use of the system and / or satisfy user requirements such as range of use for parameter settings (for example, HPLC flow). This requires close collaboration with Agilent to align the configured EQP with laboratory requirements and may include additional optional tests and/or changes to test setpoints and limits. With configured EQPs, an expanded tabular test format is used. Changes from the Agilent-recommended EQP are displayed at the individual test level (so the test section of a tabular EQP document is longer). The electronic EQP file used to create the customer configured EQP is displayed on front page of the EQP. When the qualification work is complete, the results will be reported in the Equipment Qualification Report (EQR) for review and approval.

Understanding the Test Specification Section in Tabular Review Documents

Tabular formatted EQP PDF review documents are typically used for configured EQPs (or if this format is requested by customers). When this EQP approval format is used, which applies to hardware qualifications only, tests are displayed in an expanded tabular arrangement, where the setpoints and limits are explicitly displayed for each test. Agilent-recommended setpoints and limits and the range of allowable values are designated as L (for low) and H (for high). Changes are noted relative to these limits é W (changes within the Agilent range) and O (changes outside the Agilent range). Where dual reporting limits are enables, these are designated as DW (within the Agilent limits) and DO (outside the Agilent limits). Optional tests that are enabled are included and marked as such. Additionally, any required tests that are disabled at customer request are included and marked as such. The EQP documents changes that are within the Agilent variance range as well as any out of variance range tests (see Glossary).

Note: (1) Agilent is NOT responsible for test failures for O (out of range) setpoints and limits. (2) Limit ranges must be more tightly managed than setpoint ranges because they often reflect physical measurement limits and are directly linked to the testing method. Therefore *within range* user limits are subject to best effort repairs if they cannot be met. In particular, Agilent is not be responsible for test failures for limits tighter (more demanding or challenging) than the recommended values. (3) Changes from the Agilent-recommended EQP are also displayed in the Test Summary section of the EQR. (4) For hyphenated systems (for example, LC-LCMS), an EQP for each system needs to be approved.

In a tabular EQP approval document, the test, setpoints and parameters, and limits are typically displayed in the following representative format.

Pump Flow Accuracy

Flow 1

	Analytical Agilent and non-Agilent pump							
	Setpoint:	0.500	mL/min		L:	0.100	H:	5.000
W	Setpoint:	0.200	mL/min					
	Limit:	<=	5.00	%	L:	5.00	H:	10.00

Injection Precision Additional FLD

This optional test is enabled for this EQP.

Agilent or non-Agilent injector with FLD detector							
Vial verification performed?	No						
Injection Volume on Column:	5	uL		L:	1	H:	5
Area RSD Limit:	<=	1.00	%	L:	1.00	H:	5.00
Height RSD Limit:	<=	1.00	%	L:	1.00	H:	5.00

Column Temperature Accuracy

This standard default test is disabled for this EQP.

Customer Responsibilities

To perform ACE instrument qualification services, requirements associated with instrument control and use of ACE software on site need to be understood and satisfied.

- Instrument control to perform the qualification tests.
- ACE software access by the field service engineer (FSE) to load the electronic EQP, run the qualification workflow, and publish the EQR.

ACE is designed to satisfy ALCOA+ data integrity requirements and provide qualification tests that are independent of the instrument control software. This Agilent qualification design philosophy facilitates a harmonized approach to analytical instrument qualification and ensures consistent application of validated algorithms (such as those used to perform gradient pump HPLC testing), independent of instrument and software manufacturer. Additional documentation is available to provide further information on these subjects.

Agilent recommends that the software routinely used in the lab to control the instrument is used by the FSE to perform qualification tests. Therefore, appropriate access to the instrument control software, such as the customer data system (CDS), needs to be set up for the Agilent representative before they arrive on site. For ACE software access on site, Agilent recommends installation of Network ACE to load the electronic EQP, run the qualification workflow, and publish the EQR.

Customers need to address the following responsibilities.

- EQP review
  - Review the EQP supplied (standard or configured).
  - Request changes to the EQP if required (to meet user requirements such as testing range of use) or approve the supplied EQP (that satisfies user requirements).
  - Return an electronic copy of the EQP to Agilent prior to qualification delivery.

- Agree and set up instrument control access to perform the work (provide a CDS logon for the FSE).
- Agree and approve ACE usage on site (Network ACE).
- For configured EQPs, maintain change control and revision history of the specific approved EQP.
- Safely store and archive an approved copy of this EQP.
- Review and sign the EQR when the qualification work is complete and reported.

NOTE: If Agilent representatives use customer software such as a CDS account to acquire test data during the qualification, they log off from the CDS account at the end of test acquisition. Account credentials created for FSE CDS access are a customer responsibility (that is, some labs disable the account when the work is complete).

Agilent Responsibilities

Agilent representatives follow an approved structured training process, which is represented by the training certificates included in the EQR. Additionally, any customer-specific training that is required to perform the work should be specified and complete before the work is scheduled and can be optionally added as a PDF attachment to an EQR, if required. Agilent representatives do the following.

- Deliver the approved services following the test programs described in the approved EQP;
- Provide a locked and e-signed EQR upon completion of the service;
- If requested, provide an optional ink-signed EQR CD to the customer.

Statement of Intent

The qualification is delivered according to the approved EQP. The standard EQP is followed unless a configured EQP has been requested and approved. If a configured EQP has been created and approved, Agilent defines variances as changes to the default recommended values (stated in the standard EQP) that fall within a well-defined range. These changes are considered to be within the intended use range of the system under test.

Customizations are (a) values that subject the system to limits that exceed the typical operational range or (b) additional tests that are not considered part of the core program required for completion of the selected service. Because user-defined setpoints and limits may exceed the operational envelope of the equipment, Agilent reserves the right to warrant conformance only to the closest variance value. The user is notified of this stipulation at EQP setup time and the qualification report (EQR) reflects this situation.

The service is delivered according to the terms and conditions stated in the corresponding service exhibit. After approval, it is recommended that this EQP be archived with the electronic EQP file.

General Statements on the Testing Program

The hardware OQ tests described within this EQP are designed to satisfy analytical instrument qualification (AIQ) requirements for regulated laboratories. The laboratory is responsible for documenting that analytical instruments are suitable for the analytical procedures they use and the decisions they make on the reportable values / quality attributes being measured. Diligent application of an instrument life cycle framework such as USP <1058> help define and satisfy this requirement.

Agilent-recommended EQPs are derived from Agilent's interpretation of the analytical instrument life-cycle framework defined in USP <1058> and authoritative literature requirements from sources such as ISO9001, FDA, GAMPÉ, PIC/S, ASTM 2500, and others. User requirements and intended use can vary from laboratory to laboratory. Therefore, it is recommended that prior to EQP approval, laboratories determine if additional set points and/or optional additional tests are required to test their user requirements. Additional charges may apply to any changes. This can be accommodated in a configured or customized EQP. In line with the USP <1058> requirements, Agilent qualification services include Installation Qualification (IQ) and Operational Qualification (OQ). Typically, the range of instrument use should be tested in the OQ. Laboratories are responsible for addressing PQ requirements of the USP <1058> life cycle.

Agilent CrossLab Compliance uses a balanced selection of direct metrology and chemical-based tests to directly determine the performance of the systems without unnecessary reliance on graphical extrapolation, interpolation, inferred or derived results. For example, for HPLC qualification, direct metrology measurements are used to test pump flow rate accuracy and precision, and thermal-controlled column compartment and autosampler modules. Holistic chemical testing is used for the evaluation of the following critical instrument characteristics: linearity, precision, signal to noise, and carry over.

EQP Revision History

ACE qualification protocols follow a standardized software development life cycle within Agilent. The electronic EQP files used by ACE are managed under change control within this life cycle. Changes to the core electronic EQP are recorded in the Agilent EQP Revision History and are available on request. Change control processes vary between organizations; therefore, although Agilent maintains a revision history for electronic EQPs contained within ACE, it is recommended that, for configured EQPs, laboratories maintain EQP-independent revision history information appropriate to their own policies and procedural requirements.

CDS Software Pre-requisites for Hardware Qualifications

The software used to control instruments during hardware qualification needs to be suitable. Agilent recommends that software used during the qualification has been qualified within the qualification period specified by the customer s software qualification SOP.

Glossary

Agilent EQP
ACE: Agilent Automated Compliance Engine or Agilent software used to provide qualification services

EQP:

Equipment Qualification Plan that documents qualification work to be performed

EQR:

Equipment Qualification Report that documents qualification results

CDS:

Customer data system

Network ACE:

ACE is installed on a network node within the laboratory LAN infrastructure

Local ACE:

ACE resides on an independent external drive connected to the LAN infrastructure

Alternative Method:

ACE is installed and run from a PC not connected to the laboratory network

Standard EQP:

EQP pre-defined by Agilent that includes default tests, setpoints, and limits

Configured EQP:

EQP that has been changed based on user requirements

Variance, Range:

The range of operating values for a test parameter within ACE (flow, temperature, and so on) that were defined and tested when the test was first developed and set up

Variance, W:

Change to a test parameter that is within the Agilent variance range

Variance, O:

Change to a test parameter that is outside the Agilent variance range

Variance, DW:

Dual reporting limits within the Agilent supported range

Variance, DO:

Dual reporting limits outside the Agilent supported range

Optional Test:

An optional additional test that is not included in the standard EQP

Additional Setpoint:

Additional measurement value for a test parameter (flow, temperature, and so on)

Qualification Life Cycle Stages

URS:

User Requirement Specification that documents intended instrument use

DQ:

Design Qualification that documents suitability of instrument for intended use

IQ:

Installation Qualification that documents the installation of the instrument

OQ:

Operational Qualification that tests the range of use

PQ:

Performance Qualification that tests the system under conditions of use

RQ:

Repair Qualification that tests the instrument after an instrument repair

PM:

Planned Maintenance for scheduled preventive maintenance

Reference Sources

ASTM:

American Society for Testing and Materials

FDA:

United States Food and Drug Administration

GAMPÉ:

Good Automated Manufacturing Practice

ISO:

International Organization for Standardization

ISO9001:

ISO Standard for Quality Management Systems

PIC/S:

Pharmaceutical Inspection Cooperation Scheme

USP:

United States Pharmacopeia

Dissolution Test Design and Rationale

Standard Preparation

Description: This test describes how to prepare standards for the PQ tests.

Procedure: Refer to prednisone certificate for details.

Filter Validation

Description: This test validates the filters used for sample and standard preparation.

Procedure: This test compares absorbance readings of three filtered aliquots of working standard. The % recovery for each filtered aliquot must be between 98% and 102%.

Prednisone Qualification - Single Stage

Description: This chemical test verifies the performance of the dissolution tester.

Procedure: Refer to prednisone certificate for details.

Prednisone Qualification - Two Stage

Description: This chemical test verifies the performance of the dissolution tester.

Procedure: Refer to prednisone certificate for details.

Dissolution Test Specification

DISS.02.54

This section includes (1) Agilent-recommended default setpoints and limits and (2) any customer requested change directly beneath the default. Requested changes are marked in the left margin with (1) W if within the Agilent-recommended setpoint or limit range or (2) O if outside the range. If dual limits are selected, changes are marked DW or DO. Agilent is NOT responsible for test failures for out of range setpoints and limits; they are limited to meeting the closest published allowable variance value (marked L or H) that has been exceeded. Under no conditions will Agilent be held responsible for qualification test failures that result from these user defined limits, which are therefore also excluded from the coverage of service contracts. A similar statement will also be included on the cover of related equipment qualification reports (EQRs). NOTE: Limit ranges must be more tightly managed than setpoint ranges since they often reflect physical measurement limits and are directly linked to the testing method. Therefore, *within range* user limits are subject to best effort repairs if they cannot be met. In particular, Agilent is NOT responsible for test failures for limits tighter (that is, within range but more demanding or challenging) than the recommended values.

Standard Preparation

Standard Preparation

(A working standard and a control standard are required to calculate % Absorptivity for each standard; if the customer does not want to create a control standard, % Absorptivity is NOT calculated.)

Always scheduled for supported dissolution testers: Apparatus: 1 or 2

% Absorptivity Low Limit:	>=	99.0	L:	99.0	H:	99.0
% Absorptivity High Limit:	<=	101.0	L:	101.0	H:	101.0

Filter Validation

Filter Validation

Always scheduled for supported dissolution testers: Apparatus: 1 or 2

Recovery Low Limit:	>=	98	%	L:	98	H:	98
Recovery High Limit:	<=	102	%	L:	102	H:	102

Prednisone Qualification - Single Stage

Prednisone Qualification - Single Stage1

(Limits may change with new prednisone standards. A custom EQP for the current USP lot is available.)

	Apparatus: 1; number of vessels tested 6, 7 or 8; user defined USP limits							
	Elapsed Time Setpoint:	30	minutes		L:	30	H:	30
	Geometric Mean Low Limit:	>=	81	%	L:	81	H:	81
	Geometric Mean High Limit:	<=	92	%	L:	92	H:	92
O	Geometric Mean High Limit:	<=	94	%				
	Coefficient of Variation Limit:	<=	4.6	%	L:	4.6	H:	4.6
O	Coefficient of Variation Limit:	<=	4.4	%				
	Standard Difference Limit:	<=	2.0	%	L:	2.0	H:	2.0
	Temperature Low Limit:	>=	36.5	ÁC	L:	36.5	H:	36.5
	Temperature High Limit:	<=	37.5	ÁC	L:	37.5	H:	37.5
	Sampling Accuracy Limit:	<=	2	%	L:	2	H:	2
*	Apparatus: 1 Number of vessels tested: 7 User Defined USP Limits							
	Elapsed Time Setpoint:	30	minutes		L:	30	H:	30
	Geometric Mean Low Limit:	>=	81	%	L:	81	H:	81
	Geometric Mean High Limit:	<=	92	%	L:	92	H:	92
O	Geometric Mean High Limit:	<=	94	%				
	Coefficient of Variation Limit:	<=	4.5	%	L:	4.5	H:	4.5
O	Coefficient of Variation Limit:	<=	4.3	%				
	Standard Difference Limit:	<=	2.0	%	L:	2.0	H:	2.0
	Temperature Low Limit:	>=	36.5	ÁC	L:	36.5	H:	36.5
	Temperature High Limit:	<=	37.5	ÁC	L:	37.5	H:	37.5
	Sampling Accuracy Limit:	<=	2	%	L:	2	H:	2
*	Apparatus: 1 Number of vessels tested: 8 User Defined USP Limits							
	Elapsed Time Setpoint:	30	minutes		L:	30	H:	30
	Geometric Mean Low Limit:	>=	82	%	L:	82	H:	82
O	Geometric Mean Low Limit:	>=	81	%				
	Geometric Mean High Limit:	<=	92	%	L:	92	H:	92
O	Geometric Mean High Limit:	<=	94	%				
	Coefficient of Variation Limit:	<=	4.4	%	L:	4.4	H:	4.4
O	Coefficient of Variation Limit:	<=	4.2	%				
	Standard Difference Limit:	<=	2.0	%	L:	2.0	H:	2.0
	Temperature Low Limit:	>=	36.5	ÁC	L:	36.5	H:	36.5
	Temperature High Limit:	<=	37.5	ÁC	L:	37.5	H:	37.5
	Sampling Accuracy Limit:	<=	2	%	L:	2	H:	2

	Apparatus: 2 Number of vessels tested: 6 User Defined USP Limits						
	Elapsed Time Setpoint:	30	minutes		L:	30	H: 30
	Geometric Mean Low Limit:	>=	46	%	L:	46	H: 46
O	Geometric Mean Low Limit:	>=	45	%			
	Geometric Mean High Limit:	<=	59	%	L:	59	H: 59
O	Geometric Mean High Limit:	<=	57	%			
	Coefficient of Variation Limit:	<=	6.2	%	L:	6.2	H: 6.2
O	Coefficient of Variation Limit:	<=	5.4	%			
	Standard Difference Limit:	<=	2.0	%	L:	2.0	H: 2.0
	Temperature Low Limit:	>=	36.5	ÁC	L:	36.5	H: 36.5
	Temperature High Limit:	<=	37.5	ÁC	L:	37.5	H: 37.5
	Sampling Accuracy Limit:	<=	2	%	L:	2	H: 2
*	Apparatus: 2 Number of vessels tested: 7 User Defined USP Limits						
	Elapsed Time Setpoint:	30	minutes		L:	30	H: 30
	Geometric Mean Low Limit:	>=	46	%	L:	46	H: 46
O	Geometric Mean Low Limit:	>=	45	%			
	Geometric Mean High Limit:	<=	59	%	L:	59	H: 59
O	Geometric Mean High Limit:	<=	57	%			
	Coefficient of Variation Limit:	<=	6.1	%	L:	6.1	H: 6.1
O	Coefficient of Variation Limit:	<=	5.3	%			
	Standard Difference Limit:	<=	2.0	%	L:	2.0	H: 2.0
	Temperature Low Limit:	>=	36.5	ÁC	L:	36.5	H: 36.5
	Temperature High Limit:	<=	37.5	ÁC	L:	37.5	H: 37.5
	Sampling Accuracy Limit:	<=	2	%	L:	2	H: 2
*	Apparatus: 2 Number of vessels tested: 8 User Defined USP Limits						
	Elapsed Time Setpoint:	30	minutes		L:	30	H: 30
	Geometric Mean Low Limit:	>=	46	%	L:	46	H: 46
O	Geometric Mean Low Limit:	>=	45	%			
	Geometric Mean High Limit:	<=	59	%	L:	59	H: 59
O	Geometric Mean High Limit:	<=	56	%			
	Coefficient of Variation Limit:	<=	6.0	%	L:	6.0	H: 6.0
O	Coefficient of Variation Limit:	<=	5.2	%			
	Standard Difference Limit:	<=	2.0	%	L:	2.0	H: 2.0
	Temperature Low Limit:	>=	36.5	ÁC	L:	36.5	H: 36.5

Temperature High Limit:	<=	37.5	ÁC	L:	37.5	H: 37.5
Sampling Accuracy Limit:	<=	2	%	L:	2	H: 2

Prednisone Qualification - Two Stage

Prednisone Qualification - Two Stage1

(Limits may change with new prednisone standards. A custom EQP for the current USP lot is available.)

	Apparatus: 1; number of vessels tested: 6 or 7 user defined USP limits						
	Elapsed Time Setpoint:	30	minutes		L:	30	H: 30
	Stage 1 Geometric Mean Low Limit:	>=	83	%	L:	83	H: 83
	Stage 1 Geometric Mean High Limit:	<=	90	%	L:	90	H: 90
O	Stage 1 Geometric Mean High Limit:	<=	91	%			
	Stage 1 Coefficient of Variation Limit:	<=	3.4	%	L:	3.4	H: 3.4
O	Stage 1 Coefficient of Variation Limit:	<=	3.3	%			
	Stage 1 Standard Difference Limit:	<=	2.0	%	L:	2.0	H: 2.0
	Stage 2 Geometric Mean Low Limit:	>=	81	%	L:	81	H: 81
	Stage 2 Geometric Mean High Limit:	<=	92	%	L:	92	H: 92
O	Stage 2 Geometric Mean High Limit:	<=	94	%			
	Stage 2 Coefficient of Variation Limit:	<=	4.5	%	L:	4.5	H: 4.5
O	Stage 2 Coefficient of Variation Limit:	<=	4.4	%			
	Stage 2 Standard Difference Limit:	<=	2.0	%	L:	2.0	H: 2.0
	Temperature Low Limit:	>=	36.5	ÁC	L:	36.5	H: 36.5
	Temperature High Limit:	<=	37.5	ÁC	L:	37.5	H: 37.5
	Sampling Accuracy Limit:	<=	2	%	L:	2	H: 2
*	Apparatus: 1 Number of vessels tested: 7 User Defined USP Limits						
	Elapsed Time Setpoint:	30	minutes		L:	30	H: 30
	Stage 1 Geometric Mean Low Limit:	>=	83	%	L:	83	H: 83
	Stage 1 Geometric Mean High Limit:	<=	90	%	L:	90	H: 90
O	Stage 1 Geometric Mean High Limit:	<=	91	%			
	Stage 1 Coefficient of Variation Limit:	<=	3.4	%	L:	3.4	H: 3.4
O	Stage 1 Coefficient of Variation Limit:	<=	3.3	%			
	Stage 1 Standard Difference Limit:	<=	2.0	%	L:	2.0	H: 2.0
	Stage 2 Geometric Mean Low Limit:	>=	81	%	L:	81	H: 81
	Stage 2 Geometric Mean High Limit:	<=	92	%	L:	92	H: 92
O	Stage 2 Geometric Mean High Limit:	<=	94	%			

	Stage 2 Coefficient of Variation Limit:	<=	4.4	%	L: 4.4	H: 4.4
O	Stage 2 Coefficient of Variation Limit:	<=	4.3	%		
	Stage 2 Standard Difference Limit:	<=	2.0	%	L: 2.0	H: 2.0
	Temperature Low Limit:	>=	36.5	ÁC	L: 36.5	H: 36.5
	Temperature High Limit:	<=	37.5	ÁC	L: 37.5	H: 37.5
	Sampling Accuracy Limit:	<=	2	%	L: 2	H: 2
	Apparatus: 1 Number of vessels tested: 8 User Defined USP Limits					
	Elapsed Time Setpoint:	30	minutes		L: 30	H: 30
	Stage 1 Geometric Mean Low Limit:	>=	83	%	L: 83	H: 83
	Stage 1 Geometric Mean High Limit:	<=	90	%	L: 90	H: 90
O	Stage 1 Geometric Mean High Limit:	<=	91	%		
	Stage 1 Coefficient of Variation Limit:	<=	3.4	%	L: 3.4	H: 3.4
O	Stage 1 Coefficient of Variation Limit:	<=	3.3	%		
	Stage 1 Standard Difference Limit:	<=	2.0	%	L: 2.0	H: 2.0
	Stage 2 Geometric Mean Low Limit:	>=	82	%	L: 82	H: 82
O	Stage 2 Geometric Mean Low Limit:	>=	81	%		
	Stage 2 Geometric Mean High Limit:	<=	92	%	L: 92	H: 92
O	Stage 2 Geometric Mean High Limit:	<=	94	%		
	Stage 2 Coefficient of Variation Limit:	<=	4.3	%	L: 4.3	H: 4.3
O	Stage 2 Coefficient of Variation Limit:	<=	4.2	%		
	Stage 2 Standard Difference Limit:	<=	2.0	%	L: 2.0	H: 2.0
	Temperature Low Limit:	>=	36.5	ÁC	L: 36.5	H: 36.5
	Temperature High Limit:	<=	37.5	ÁC	L: 37.5	H: 37.5
	Sampling Accuracy Limit:	<=	2	%	L: 2	H: 2
*	Apparatus: 2 Number of vessels tested: 6 User Defined USP Limits					
	Elapsed Time Setpoint:	30	minutes		L: 30	H: 30
	Stage 1 Geometric Mean Low Limit:	>=	48	%	L: 48	H: 48
O	Stage 1 Geometric Mean Low Limit:	>=	47	%		
	Stage 1 Geometric Mean High Limit:	<=	57	%	L: 57	H: 57
O	Stage 1 Geometric Mean High Limit:	<=	54	%		
	Stage 1 Coefficient of Variation Limit:	<=	4.6	%	L: 4.6	H: 4.6
O	Stage 1 Coefficient of Variation Limit:	<=	4.1	%		
	Stage 1 Standard Difference Limit:	<=	2.0	%	L: 2.0	H: 2.0
	Stage 2 Geometric Mean Low Limit:	>=	46	%	L: 46	H: 46

O	Stage 2 Geometric Mean Low Limit:	>=	45	%			
	Stage 2 Geometric Mean High Limit:	<=	59	%	L:	59	H: 59
O	Stage 2 Geometric Mean High Limit:	<=	57	%			
	Stage 2 Coefficient of Variation Limit:	<=	6.1	%	L:	6.1	H: 6.1
O	Stage 2 Coefficient of Variation Limit:	<=	5.4	%			
	Stage 2 Standard Difference Limit:	<=	2.0	%	L:	2.0	H: 2.0
	Temperature Low Limit:	>=	36.5	ÁC	L:	36.5	H: 36.5
	Temperature High Limit:	<=	37.5	ÁC	L:	37.5	H: 37.5
	Sampling Accuracy Limit:	<=	2	%	L:	2	H: 2
*	Apparatus: 2 Number of vessels tested: 7 User Defined USP Limits						
	Elapsed Time Setpoint:	30	minutes		L:	30	H: 30
	Stage 1 Geometric Mean Low Limit:	>=	48	%	L:	48	H: 48
O	Stage 1 Geometric Mean Low Limit:	>=	47	%			
	Stage 1 Geometric Mean High Limit:	<=	57	%	L:	57	H: 57
O	Stage 1 Geometric Mean High Limit:	<=	54	%			
	Stage 1 Coefficient of Variation Limit:	<=	4.6	%	L:	4.6	H: 4.6
O	Stage 1 Coefficient of Variation Limit:	<=	4.1	%			
	Stage 1 Standard Difference Limit:	<=	2.0	%	L:	2.0	H: 2.0
	Stage 2 Geometric Mean Low Limit:	>=	46	%	L:	46	H: 46
O	Stage 2 Geometric Mean Low Limit:	>=	45	%			
	Stage 2 Geometric Mean High Limit:	<=	59	%	L:	59	H: 59
O	Stage 2 Geometric Mean High Limit:	<=	57	%			
	Stage 2 Coefficient of Variation Limit:	<=	6.0	%	L:	6.0	H: 6.0
O	Stage 2 Coefficient of Variation Limit:	<=	5.3	%			
	Stage 2 Standard Difference Limit:	<=	2.0	%	L:	2.0	H: 2.0
	Temperature Low Limit:	>=	36.5	ÁC	L:	36.5	H: 36.5
	Temperature High Limit:	<=	37.5	ÁC	L:	37.5	H: 37.5
	Sampling Accuracy Limit:	<=	2	%	L:	2	H: 2
*	Apparatus: 2 Number of vessels tested: 8 User Defined USP Limits						
	Elapsed Time Setpoint:	30	minutes		L:	30	H: 30
	Stage 1 Geometric Mean Low Limit:	>=	48	%	L:	48	H: 48
O	Stage 1 Geometric Mean Low Limit:	>=	47	%			
	Stage 1 Geometric Mean High Limit:	<=	57	%	L:	57	H: 57
O	Stage 1 Geometric Mean High Limit:	<=	54	%			

	Stage 1 Coefficient of Variation Limit:	<=	4.6	%	L: 4.6	H: 4.6
O	Stage 1 Coefficient of Variation Limit:	<=	4.1	%		
	Stage 1 Standard Difference Limit:	<=	2.0	%	L: 2.0	H: 2.0
	Stage 2 Geometric Mean Low Limit:	>=	46	%	L: 46	H: 46
O	Stage 2 Geometric Mean Low Limit:	>=	45	%		
	Stage 2 Geometric Mean High Limit:	<=	59	%	L: 59	H: 59
O	Stage 2 Geometric Mean High Limit:	<=	56	%		
	Stage 2 Coefficient of Variation Limit:	<=	5.9	%	L: 5.9	H: 5.9
O	Stage 2 Coefficient of Variation Limit:	<=	5.2	%		
	Stage 2 Standard Difference Limit:	<=	2.0	%	L: 2.0	H: 2.0
	Temperature Low Limit:	>=	36.5	ÁC	L: 36.5	H: 36.5
	Temperature High Limit:	<=	37.5	ÁC	L: 37.5	H: 37.5
	Sampling Accuracy Limit:	<=	2	%	L: 2	H: 2

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DISSOLUTION PERFORMANCE VERIFICATION STANDARD - PREDNISONE

(10 mg nominal prednisone content per tablet)

USP Catalog No.:	1222818
USP Lot No.:	R182R0

Valid Use Date	31-JUL-2025
Storage/Handling	As per the label.
Uses	General Chapter <711> Dissolution, Performance Verification Test (PVT), Apparatus 1 and Apparatus 2

Dissolution <711>

Medium:	499 g of degassed purified water maintained at 37° ± 0.5°
Medium degassing:	Recommended degassing procedure: Heat a suitable amount of water, while stirring gently to about 41-45°. Filter under vacuum through a 0.45-µm-porosity filter into a suitable filtering flask equipped with a stirring device. Seal the flask and continue to apply vacuum while stirring for an additional five minutes. Measured vacuum should be less than 100 mbar. **Note**: Other validated degassing methods that reduce the total dissolved gas in the media can also be used
Apparatus:	Apparatus 1 (Basket) or Apparatus 2 (Paddle) at 50 RPM Note: If equipment is dedicated for use with only one apparatus (basket or paddle), then performance verification is only required for that apparatus
Time:	30 minutes
Standard Solution:	A known concentration of USP Prednisone RS in Medium. **Note**: An amount of alcohol not to exceed 5% of the total volume of the standard solution may be used to bring the prednisone reference standard into solution.
Sample solution:	Laboratory can choose either Single-Stage Test or Optional Two-Stage Test scheme to obtain Sample Solutions. A filtered portion of the solution under test, suitably diluted, if necessary, with Medium to obtain a concentration similar to that of the Standard solution. **Note 1**: The filtering method must not cause adsorptive loss of drug **Note 2**: Bias introduced by automated methods is to be avoided
Analysis:	UV at maximum absorbance of about 242 nm
Procedure:	Determine the quantity of prednisone, $C_{21}H_{26}O_5$, dissolved at 30 minutes in each vessel expressed as percent of the labeled amount.

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Single-Stage Test Instructions and Acceptance Criteria

1. For each position in the assembly, test one USP Dissolution Performance Verification Standard – Prednisone (DPVS – Prednisone) RS tablet, and record the percent dissolved at the sampling time point specified. Transform the percent dissolved results to the natural log scale, determine the mean and variance. For assemblies with 12 or 14 dissolution vessels, no further testing is required
2. For assemblies with fewer than 12 positions, repeat Step 1 with an additional set of tablets. Transform the percent dissolved results to the natural log scale, determine the mean and variance.
3. Calculate the average of the two means and of the two variances obtained in Steps 1 and 2.
   Use the results from Step 1 alone for assemblies that have 12 or 14 positions.
4. Convert the results of Step 3 to a geometric mean (GM) and percent coefficient of variation (%CV). See Calculation Example for details.
5. Compare the results of Step 4 to the Single-Stage acceptance criteria in Table 1. The GM must not fall outside the limits, and the %CV must not be greater than the limit. If both meet the criteria, the assembly has passed the PVT

Table 1. Performance Verification Test Acceptance Criteria for Single-Stage Test

Apparatus	No. of vessels per run	Geometric Mean, % Prednisone Dissolved	%CV
1 (Basket)	6	81-94	4.4
	7	81-94	4.3
	8	81-94	4.2
	12	81-94	4.3
	14	81-94	4.3
2 (Paddle)	6	45-57	5.4
	7	45-57	5.3
	8	45-56	5.2
	12	45-57	5.4
	14	45-57	5.3

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Optional Two-Stage Test Instructions and Acceptance Criteria

A laboratory may choose to implement the PVT as a Two-Stage test in case of assemblies with less than 12 positions. The Two-Stage test is a statistically valid means of allowing the possibility of stopping the test at the first stage using more stringent acceptance criteria. The following are step-by-step instructions for the two-stage test

1. For each position in the assembly, test one USP DPVS – Prednisone RS tablet, and record the percent dissolved at the sampling time point specified. Transform the percent dissolved results to the natural log scale, determine the mean and variance
2. Convert the results of Step 1 to a GM and %CV and compare to the 1st Stage of Two Stages acceptance ranges in Table 2. The GM must not fall outside the limits, and the %CV must not be greater than the limit. For calculation of the GM and %CV, see Calculation Example for details
3. If results of Step 2 satisfy both acceptance criteria, the assembly has passed the PVT. Otherwise continue to Step 4. Prior to proceeding to Step 4, see Futility Factor section.
4. Repeat Step 1 with an additional set of tablets. Transform the percent dissolved results to the natural log scale determine the mean and variance for the data obtained at this step
5. Average the two means and two variances obtained in Steps 1 and 4
6. Convert the results of Step 5 to a geometric mean (GM) and percent coefficient of variation (%CV). For calculation of the GM and %CV, see Calculation Example for details
7. Compare the results of Step 6 to the 2nd Stage of Two Stages acceptance ranges in Table 2. The GM must not fall outside the limits, and the %CV must not be greater than the limit. If both meet the acceptance criteria, the assembly has passed the PVT

Table 2. Performance Verification Test Acceptance Criteria for Two-Stage Test

Apparatus	No. of vessels per run	First Stage of Two-Stage Test		Second Stage of Two-Stage Test	
		Geometric Mean, % Prednisone Dissolved	%CV	Geometric Mean, % Prednisone Dissolved	%CV
1 (Basket)	6	83-91	3.3	81-94	4.4
	7	83-91	3.3	81-94	4.3
	8	83-91	3.3	81-94	4.2
2 (Paddle)	6	47-54	4.1	45-57	5.4
	7	47-54	4.1	45-57	5.3
	8	47-54	4.1	45-56	5.2

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Futility Factor

If optional Stage-Two test is chosen, there are circumstances when the %CV after the First Stage of Two-Stage test equals or exceeds the value in the Futility Factor table (without rounding). In such cases it is impossible to meet the %CV criterion after the Second Stage of the Two-Stage test. The lab can stop after the First Stage run. However, after any adjustments to equipment, test procedure, and so on, the PVT must be restarted with a new first run (Step 1 of the two-stage test instructions).

Futility Factor, %CV at or above value given, second stage testing will not produce passing result

Apparatus	Number of Vessels		
	6	7	8
1	6.2	6.1	5.9
2	7.6	7.5	7.4

Refer to this website for the USP Calculation Tool: https://apps.usp.org/app/USPNF/pvtCalculationTool/

Calculation Example (expressed as Microsoft Excel® worksheet functions)**:**

Run 1: $x_1, x_2, \ldots, x_n$ in natural log scale: Ln x_1, Ln x_2, …, Ln x_n

Run 2: $x_{n+1}, x_{n+2}, \ldots, x_{2n}$ in natural log scale: Ln x_{n+1}, Ln x_{n+2}, …, Ln x_{2n}

1st Stage of Two-Stage for n=6, 7, 8 and Single-Stage for n=12, 14:

GM1 = exp(average (Ln x_1:Ln x_n))

%CV1 = 100*sqrt(exp(var(Ln x_1:Ln x_n)) -1)

Single-Stage or 2nd Stage of Two-Stage for n= 6, 7, 8:

GM = exp(average((average (Ln x_1:Ln x_n)), (average (Ln x_{n+1}:Ln x_{2n})))) = exp(average (Ln x_1:Ln x_{2n}))

%CV= 100*sqrt(exp(average((var(Ln x_1:Ln x_n)),(var(Ln x_{n+1}:Ln x_{2n})))) -1)

exp: exponential (e^x) var: variance sqrt: square root *: multiply 100: conversion factor to percentage

For more information and guidelines about how to complete the performance verification test refer to the following website: https://www.usp.org/small-molecules/pvt

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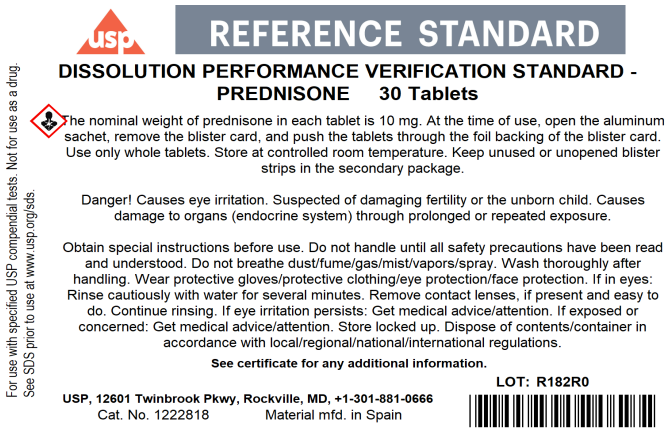
Label



Danielle A. Vattimo

Quality Assurance

Certificate Version History

Version Number	Date	Reasons for Change
00 (Current)	14-MAR-2024	First issue

USP Reference Standard Certificate Template No.: FORM-00008-02
Template Effective Date: 15-DEC-2023

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Label

Reference Standard label typically contains the name, catalog number, lot number, package size, assigned value when applicable, storage conditions, handling instructions, and country of origin information. The label may also include hazard and precautionary statements required by the Occupational Safety and Health Administration (OSHA).

Assigned Value

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DISSOLUTION SYSTEMS PERFORMANCE QUALIFICATION

Agilent CrossLab Compliance Services

Standard PQ Test Suite

This document describes the test program for qualifying dissolution instruments, and the following tables list all PQ tests. PQ affirms that your dissolution apparatus performs in accordance with current USP requirements. The USP Dissolution Performance Verification Test (PVT) is performed as required in the current USP General Chapters, Dissolution <711> and Drug Release <724>, in accordance with cGMPs.

Note: The actual test limits are subject to change when a new prednisone standard is released. A custom EQP is available with limits for the current USP lot.

Test	Setpoints and Parameters	Limits
Standard Preparation	N/A	% Absorbtivity ≥ 99.0% and ≤ 101.0% for working and control standards (calculations are performed only if the control standard is used)
Filter Validation	N/A	Recovery ≥ 98% and ≤ 102% for each filtered aliquot
Prednisone Qualification (All variations of test)	Vessel temperature: 37.0°C Elapsed time: 30 minutes (target window from tablet drop to sampling)	See current USP lot's Certificate of Analysis

Consumables, Supplies, and Parts Used for Qualification

All parts, supplies, standards and consumables specified by the Agilent qualification protocol are provided by the customer. Agilent does not provide Prednisone standards due to the impact of improper storage, which can adversely affect the potency and/or purity of the standards and put the integrity of the qualification at risk. Agilent will provide equipment necessary for the measurement of physical parameters (e.g., thermometer, level, tachometer, wobble gauge, etc.). Any additional parts for maintenance or repair needed to affect qualification will be billed to customer unless otherwise covered by Agilent service and support agreement.

Test Design and Rationale

PQ service does not include physical testing (e.g., measurements of speed, wobble, centering, level, etc.). Because the physical condition of the Dissolution tester can affect the outcome of the Performance Qualification, it is recommended that an inspection of the equipment and measurements of physical parameters are performed prior to the service to ensure that the equipment conforms to pharmacopeia requirements.

Standard Preparation

Description: This test describes how to prepare standards for the PQ tests.

Procedure: Refer to prednisone certificate for details

Filter Validation

Description: This test validates the filters used for sample and standard preparation.

Procedure: This test compares absorbance readings of three filtered aliquots of working standard.

Prednisone Qualification

Description: These chemical tests verify the performance of the dissolution tester.

Procedure: Refer to prednisone certificate for details.

www.agilent.com/chem/qualification

Report and Delivery Options

This list below includes options selected for inclusion in the EQR. By default, repeated run logs and transaction logs are always included; all other options can be included or excluded.

(For hyphenated system types only) If different options are chosen for the primary and supported system types, the primary system options are used for both techniques.

- Show chromatograms
- Show header and footer on cover
- Include repeated run logs
- Include Transaction logs

Selected Signature Options

Status: EQP is not locked

- Reporting variance is allowed in this EQP

Customer Approval

Name:	
Title:	
Date:	
Signature:	

Name:	
Title:	
Date:	
Signature:	

Name:	
Title:	
Date:	
Signature:	

Name:	
Title:	
Date:	
Signature:	

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Agilent CrossLab Compliance and its primary components (ACE software tool, procedures, test design, metrology tools, chemical reference standards, and operator training materials) have been designed, tested, validated, and released for commercial use following Agilent's Life Cycle Development Quality Assurance methodology. A review of the following life cycle stages is a key part of the ACE software and associated protocol development process.

-Product Description / Specification
-Life Cycle Phases / Transition Approval
-Quality Assurance / Testing
-Documentation and Change Management
-Source Code

Validation certificates for the ACE software and associated protocols are generated automatically as part of the life cycle process, prior to software release, and are available on request. The certificate includes a declaration of intent statement and is representative of the life cycle process followed.

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